ABC of allergies
Diagnosing allergy

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Allergy to environmental agents can affect almost every organ of the body. Although allergic rhinitis is the commonest manifestation, the lower respiratory tract, the conjunctiva, the skin, and the gastrointestinal tract are frequently affected by allergic disease.

Allergic diseases are common, and their prevalence is increasing. Accurate diagnosis of triggering or causative allergens is essential for appropriate advice for avoidance and environmental control measures. Although allergic diseases can occur at almost any age, some allergies are most likely to develop for the first time in particular age groups.

Age when certain allergies are likely to occur for first time

- Neonates—Atopic dermatitis, food allergies (milk, egg, nuts)
- Early childhood—Asthma (house dust mite, pets)
- Teenagers—Allergic rhinitis (grass and tree pollens)
- Early adulthod—Urticaria, angio-oedema (aspirin intolerance)
- Adulthood—Allergy to venom (bee, wasp); nasal polyps

Symptoms

An immediate relation between exposure to potential allergens and the development of symptoms makes both the diagnosis and identification of allergy straightforward. In 25-50% of cases the predominant symptoms develop 1-10 hours after exposure (late phase reactions), obscuring the allergic nature of the illness. In allergic diseases of occupational aetiology the first symptom may be exercise induced asthma or night-time waking with cough. The longer such symptoms have been present the more likely they are to persist when exposure ceases.

The onset of seasonal symptoms occurs three weeks earlier in southern England than in northern Scotland.

Symptoms occur more rapidly after exposure to the causative agent as sensitisation increases. Many patients with food allergy develop either a craving for or an intense dislike of the offending food. Symptoms are usually gastrointestinal (abdominal pain, bloating, vomiting, diarrhoea) or cutaneous (itching, urticaria, angio-oedema)—symptoms are less commonly respiratory (asthma) and are rarely related to rhinitis.

Cross reaction can occur between various allergens, such as birch tree pollen and certain foods (for example, apple, carrot, celery, potato, orange, tomato, hazelnut, and peanut). Cross reactivity also exists between latex and some fruits (banana, avocado, kiwi fruit, and chestnut).

Itching of the throat and ears is a common manifestation of pollen allergy, and patients allergic to house dust mite experience exacerbations when bedmaking, vacuum cleaning, and sleeping in damp accommodation.

The impact of the allergic symptoms on an individual's lifestyle should be assessed in terms of impairment of school or work performance and time missed, with particular emphasis on the interference in leisure activities and sleep.

Taking a clinical history

- A detailed clinical history is vital for diagnosing an allergy
- Taking a history requires experience, time, and patience
- Patients should be allowed to give their own account of their symptoms in their own time
- Structured questions about the patients' history (with particular emphasis on previous allergic diseases—such as childhood eczema, hay fever, and asthma) should be asked
- Frequency, severity, duration, and seasonality of symptoms should be ascertained, with particular reference to triggering factors, life threatening events, and effects of avoidance measures
- Patients should be asked about diet; food exclusion; and intolerance to aspirin, colourings, and preservatives
- Family history should be explored
- Home, work, and outdoor environmental risk factors should be discussed
- Groups at particular risk of allergy—such as healthcare and rubber industry workers and children with spina bifida, in whom latex allergy is particularly prevalent—should be identified
- Patients should be asked about any treatment they are currently using, particularly about antihistamines, topical and oral corticosteroids, and adrenalin autoinjectors

Factors influencing development of allergic diseases

If both parents are allergic the risk of allergy in the offspring is 75%; if one parent is allergic the risk is 50%. The risk in the population is 10-20%. Allergy is much less common in younger children in large families than in their older siblings. This is probably due to viral infections being passed more often from one child to another in large families, which may influence the subsequent dominance of Th1 driven rather than Th2 driven immune responses.

Environmental factors predisposing to development and triggering of allergy

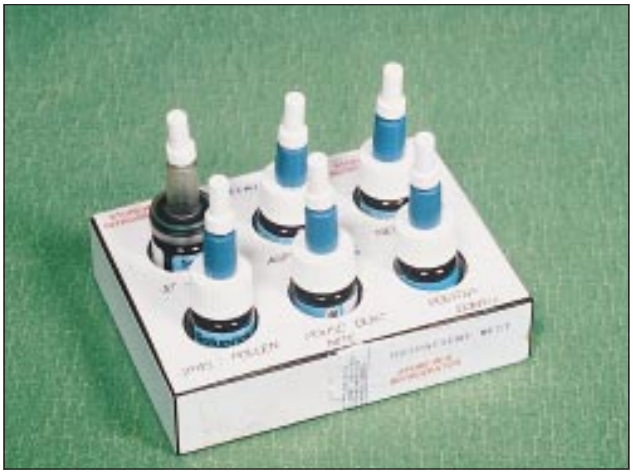
Indoor
Damp and poorly ventilated dwelling
Old mattresses (not vacuumed or covered)
Unwashed and uncovered pillows and duvet
Pets
Cigarette smoke
Gas fired cooking stoves, boilers, and fires (not adequately ventilated to the outside)

Outdoor
Density of grains of grass or tree pollen in local environment
Presence of new aeroallergens—eg *Parietaria judaiica* (the wall pellitory) in southern England
Proximity to major roadways or power stations

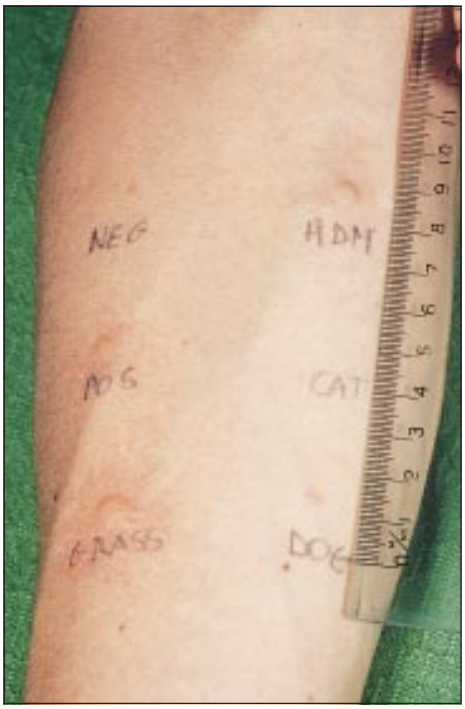
Occupational
Isocyanate
Flour
Laboratory animals
Resin
Wood dust
Glutaraldehyde
Biological enzymes
Latex

Allergy tests in vivo

Lancet for skin prick testing



Skin prick test kit comprising four allergens and positive control solution (histamine 10 mg/ml) and negative control (allergen diluent)



Evaluation at 15 minutes of skin prick test results (weal sizes in mm)

Skin tests

Skin prick test

The skin prick test is the most widely used allergy test and can be performed during the initial consultation with aqueous solutions of a variety of allergens. These include *(a)* common inhaled allergens (house dust mite, grass pollen, cat dander, dog hair); *(b)* occupational allergens (such as ammonium persulphate, platinum salts, antibiotics, and latex); and *(c)* food allergens

Skin prick testing requires control using diluent (negative control) and histamine solution (positive control). A drop of allergen solution is placed on the skin of the forearm. A sterile lancet or 25 gauge (orange) needle is used to prick the skin through the allergen solution (a separate needle is used for each allergen solution). The excess allergen solution is removed from the skin with an absorbent paper tissue. The reaction is evaluated after 15 minutes.

The test should be performed with standardised allergen solutions, if possible. In general practice it may be sufficient to use four allergens (house dust mite, grass pollen, and cat and dog allergen) plus the positive and negative controls to confirm or exclude atopy and recognise the most common allergens encountered.

Test solutions are available from ALK Abello (Reading, Berkshire) under the brand name Soluprick.

A positive result is a skin weal >2 mm greater than that observed with the negative control (allergen diluent) solution. However, the relation between a positive result and overt clinical disease caused by that allergen is not absolute. The concentration of the allergen solution will determine the result of the test. Ideally the test should combine the highest possible sensitivity with the highest possible specificity, but this degree of precision is not usually achievable.

The result of the skin prick test should be interpreted in the light of the clinical history: if both the history of allergy and the test result are positive, atopy and the offending allergen are confirmed; if both are negative, allergy is excluded; in the case of perennial allergens, there may not be an immediate association between exposure and symptoms, resulting in a false negative history in the context of a positive test result; many patients with a positive test result do not have symptoms of allergy; if there is discordance between the history and the test result, referral to an allergy specialist is recommended.

The advantages of skin prick testing are: it is painless and has a low risk of side effects; it is informative to the patient; patient compliance is high; and the test can be performed in health centres.

The disadvantages are: systemic and topical antihistamines may suppress the weal and flare reaction; the test is less reliable with food allergens (which are less well standardised) than with inhaled allergens; itching causes a slight discomfort; and interpretation is difficult in patients with eczema or dermatographism.

Although skin prick testing with inhaled allergens is generally safe, occasional systemic reactions including anaphylaxis have been reported when food allergens are used; testing with food allergens should therefore be performed only in specialist centres. Adrenaline should always be available.

Intracutaneous test

The intracutaneous test is rarely indicated, though it is of value in the diagnosis of drug or venom allergy.

It should be performed by allergy specialists in specialist centres.

Patch test

The patch test is widely used in the diagnosis of allergic contact dermatitis. Several standardised series of contact allergens are available. Possible allergens are applied in a standardised form to a healthy area of the patient's skin. The patch test can be performed either with the suspected chemicals or with the standard series of allergens.

Eczematous reaction at the site of application 48-72 hours later shows that the patient is sensitised to that allergen. The reaction must be distinguished from simple irritant reactions.

The patch test is the most important diagnostic tool in diagnosing contact allergic dermatitis. However, patch testing can cause a flare up reaction (of healed eczema) or persisting test reactions. It can also cause sensitisation and subsequent allergic contact dermatitis. It is time consuming, and it requires specialist interpretation.

Common examples of contact allergy

Agent	Source
Mercury	Topical ointments
Copper	Coins, jewellery, door handles
Nickel	Coins, alloys, insecticides
p-Phenylenediamine	Hair dye, fur dye
Paraben	Cosmetics
Imidazolidinyl urea	Cosmetics (preservatives)
Formalin, formaldehyde	Cosmetics, insecticides
Carba mix	Rubber, fungicides
Thiuram	Rubber compounds, fungicides
Epoxy resin	Adhesives

Bronchial, nasal, and conjunctival provocation tests

These tests are rarely required in the routine diagnosis of allergy. Bronchial or nasal provocation test with allergen may occasionally be useful in determining "local sensitisation," in which, although the results of skin prick testing (and of the radioallergosorbent test, if also done) are negative, the airways are responsive to the specific allergen. These tests must be performed only by individuals trained in allergy diagnosis.

Food challenge

Diagnosis of food allergy requires taking a careful history and, if necessary, altering the patient's diet with the help of a skilled dietician. The consequence of correct diagnosis can be beneficial to patients but may disrupt their lifestyle. A definite diagnosis of food allergy can be established by properly conducted blinded food challenges, which avoid any possible bias from patient or investigator.

Food challenge will be covered in more detail in a later chapter on food allergy.

Food challenge

- Removal of the food from the patient's diet should eliminate symptoms
- Ideally challenges should be conducted as double blind, placebo controlled challenges
- If the suspected food, but not the inactive substance, causes an allergic reaction, the diagnosis is established
- Food challenges must be performed under strict medical supervision and in hospital settings
- Food challenges, however, may cause anaphylactic reaction, are time consuming, and require several challenges, with washout periods of days

Allergy tests in vitro

Nasal smears

Nasal smear tests are used to determine the number of eosinophils present in the nasal secretion. A cotton bud is inserted two or three times into each nostril, and the lining of the nose scraped with a firm, rolling movement. Secretions are spread gently on to a microscope slide and stained, and the cells are counted.

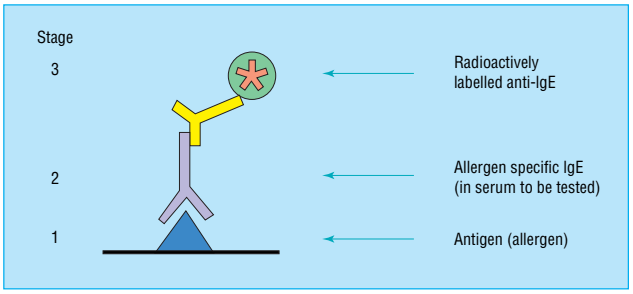
The advantages of nasal smears are that the nose is readily accessible and the test can help to differentiate between eosinophilic rhinitis (allergic rhinitis and non-allergic rhinitis with eosinophilia, which respond well to topical corticosteroids) and rhinitis due to other causes. However, the disadvantages are a slight discomfort to the patient and a high risk of false negative results if the nasal smear is not properly obtained.

If more than 10% of the stained cells in nasal smears are eosinophils this indicates a positive result compatible with nasal eosinophilia

Serum allergen specific IgE concentrations

In the radioallergosorbent test (RAST) allergens (antigens) are chemically bound to an insoluble matrix such as plastic, cellulose nitrate, cellulose (paper), or agarose beads. When patients' serum is added, allergen specific IgE binds to immobilised allergen. Radioactively labelled anti-IgE is then added, which attaches to the specific IgE already bound to the allergen. The amount of specific IgE in the patient's blood can be estimated from the amount of bound radioactivity.

In another type of radioallergosorbent test (the CAP-RAST) system) the allergen is covalently coupled to a cellulose carrier



The principle of the radioallergosorbent test

with a large surface area. The patient's serum containing IgE is then added and specific IgE reacts with bound allergen. After non-specific IgE has been washed away, enzyme labelled antibodies against human IgE are added, and the bound complex is then incubated with a fluorescence substrate, the developing agent.

An enzyme linked immunosorbent assay (ELISA) is a non-radioactive method which uses antigen in fluid phase and enzyme labelling of anti-IgE, which is detected by adding substrate for the enzyme, which produces colour change detected photometrically.

The radioactivity (radioallergosorbent test), fluorescence (CAP-RAST test), or colour (enzyme linked immunosorbent assay) of the eluate corresponds with the concentration of specific IgE in the patient's blood.

The advantages of measuring the concentration of allergen specific IgE are that *(a)* it is not influenced by any concurrent drug treatment, *(b)* it can be performed when there is widespread skin disease, *(c)* it is completely safe, *(d)* the specificity of the two radioallergosorbent tests can be as high as 90% for inhaled allergens. However, the results are not immediately available, and testing is expensive.

Alternative tests

- Recently there has been a surge in the number of alternative "allergy tests" offered direct to patients—for example, the antigen leucocyte cellular antibody test, hair analysis, bioresonance diagnostics, autohomologous immune therapy, electroacupuncture, and vega testing
- No scientific evidence exists that these tests are useful in diagnosing allergy
- Such tests may also disadvantage patients, who may modify diet and lifestyle to no avail

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The ABC of allergies is edited by Stephen Durham, honorary consultant physician in respiratory medicine at the Royal Brompton Hospital, London. It will be published as a book towards the end of 1998.

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A lesson learnt

Always listen to the patient

It was almost 3 00 pm and I was at home trying hard to sleep off the effects of a set of nights on call as a senior house officer in paediatrics when I was awoken by my worried wife and presented with our 4 year old child, Steven. Sleepily, I took a quick bedside history. My wife and two sons had been to the fairground in the morning. Steven had been apparently well, but had been complaining of pain "in his willy" since lunchtime, and when she eventually examined him she was alarmed to find that his scrotum was massively swollen.

From my bed and with only a halfhearted glance at my son, I decided that swollen testicles merited a turf to the surgeons. Two telephone calls later they were on the way to the casualty department to see a surgical colleague. I followed along blearily and eventually met up with everyone in the *x* ray department, where a kindly radiologist was ultrasounding his scrotum. Fifteen minutes later, much relieved by the gentle whooshing of the doppler, we were gratefully leaving hospital, and I was busy explaining to Steven (despite his protests to the contrary) that he must have banged himself "down below."

Later that evening, despite the panacea of paracetamol, he wouldn't eat his dinner because his tummy hurt. With the minimum of sympathy I explained that this was his poorly willy and he was bundled off to bed.

He felt sufficiently recovered by the next day for us to continue with our plans to take a trip to the Lake District to see his grandparents. The eye of faith confirmed that his scrotum was much less swollen and so we proceeded to endure the monotony of the M6, the journey being punctuated with only occasional complaints of tummy pain.

The evening saw a return of both his usual good humour and appetite (attributed to Grandma's cooking) and at bathtime a cursory examination revealed two flea bites on his right ankle and two non-blanching spots on his right thigh. Smiling and playful, he was put to bed.

The next morning, for the second time in two days I was woken and presented with my son, the patient. His Grandma had woken to find him crying and complaining of pain in his left arm, which he was refusing to use. A quick examination revealed a swollen and tender left elbow. I guiltily recalled swinging him around like an aeroplane the evening before—much to his delight at the time. I mentally rehearsed the inevitable embarrassing scene to follow in the casualty department as I explained how he had hurt his elbow.

Clearing the sleep from my eyes and hurriedly throwing on a few clothes, I cast my mind back to the rash I had noticed the previous evening. I called Steven over to my bedside and a quick check revealed a rather familiar purpuric rash down both thighs and now spreading across his buttocks. My moment of diagnostic triumph was shortlived as with horror I recalled attending a child with Henoch Schönlein purpura only a few weeks beforehand and reassuring his parents about his bruised and swollen testicles. The penny may have dropped, but it took almost two days to fall.

In retrospect, I have been reminded of three important points of clinical practice. Firstly, always listen to the patient, especially when the answers do not fit with your working diagnosis. Secondly, always complete a thorough physical examination; there may be unlooked for clues that will lead you to an early diagnosis. Finally, and most importantly, whatever else happens, you can always rely on your children to confuse, confound, and ultimately embarrass you.

William D Carroll, *senior house officer in paediatrics, Northampton*

We welcome articles up to 600 words on topics such as *A memorable patient, A paper that changed my practice, My most unfortunate mistake,* or any other piece conveying instruction, pathos, or humour. If possible the article should be supplied on a disk. Permission is needed from the patient or a relative if an identifiable patient is referred to. We also welcome contributions for "Endpieces," consisting of quotations of up to 80 words (but most are considerably shorter) from any source, ancient or modern, which have appealed to the reader.